The Patient-Centered Outcomes Research Network:
A National Infrastructure for Comparative Effectiveness Research

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The current clinical research system does not produce high-quality evidence quickly enough to support health care decision making. The Patient-Centered Outcomes Research Network (PCORnet) embodies a novel strategy for creating a national "network of networks" that is capable of significantly accelerating evidence generation to support a learning health system.

The Patient-Centered Outcomes Research Network (PCORnet) [1] represents the confluence of several evolving concepts in clinical care and biomedical research. First among these is the view that patients should be involved in the prioritization, design, conduct, analysis, interpretation, and dissemination of research. Second is the belief that patients, caregivers, health care providers, and systems will be able to make better decisions about health and health care if they have access to high-quality, relevant comparative data about therapies and treatment strategies. Third, as our understanding of the need for evidence to support clinical decision making has evolved, the Institute of Medicine of the National Academies and others have championed the concept of the *learning health system* [2], in which research and care are integrated to drive a cycle of continuous learning and improvement.

PCORnet also represents a response to widespread frustration with the current clinical research system [2], which is producing reliable evidence at only a fraction of the rate needed to meaningfully inform the decisions of system stakeholders. For example, a study of cardiovascular practice guidelines found that most (about 88%) of the clinical recommendations included in these guidelines were not based on high-quality evidence [3]. Furthermore, the limitations imposed by the costs and inefficiencies of clinical trials were acknowledged more than a decade ago [4], and numerous entities have since attempted to address these problems [5, 6].

In 2002 the National Institutes of Health (NIH) convened stakeholders to discuss problems facing medical research, and the NIH Roadmap for Medical Research was launched in 2004 [7]. This roadmap included a call for the construction of a national system that would allow research activities to be conducted in the context of clinical care with the full participation of patients, their families, and care providers (see Table 1); this system would use electronic health records (EHRs) as its major source of data. The NIH projected that such a plan would take more than a decade to create and implement and concluded that it could not support the full cost of such a network. The NIH ultimately decided to fund the Clinical and Translational Science Award (CTSA) program to provide infrastructure and training for clinical and translational research [8], but it specifically decided not to fund a national clinical research network. PCORnet, which is funded by a nongovernmental organization (the Patient-Centered Outcomes Research Institute [PCORI]), works in concert with the CTSA infrastructure and training system and has specific alliances with multiple components of the NIH.

These programs have been complemented by other efforts such as the Clinical Trials Transformation Initiative (CTTI). CTTI is a nonprofit public-private partnership that includes representatives from the US Food and Drug Administration (FDA) and more than 60 academic, industry, volunteer, and government organizations. CTTI's efforts are predicated on the belief that incremental improvements in the clinical research system are insufficient to meet stakeholder needs and that transformational change is therefore required [5].

Amid this ferment, PCORI, which is an independent, congressionally authorized institute, articulated a vision for a new type of national network for comparative effectiveness clinical research—PCORnet. In 2013 PCORI released a request for proposals for a coordinating center and announced a funding opportunity for multiple networks to form a national "network of networks" that could provide the needed transformational change. PCORnet is not intended

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TABLE 1.
A Plan for Reengineering the Clinical Research Enterprise: The National Institutes of Health (NIH) Roadmap

Goals for years 1–3	Goals for years 4–7	Goals for years 8–10
	Lowest level of difficulty	
• Plan and start a few demonstration clinical research networks. • Carry out demonstration projects to show how complex regulatory systems might be simplified. • Put a plan in place for clinical research networks for all NIH institutes.	• Create a funding mechanism to sustain a national system through consensus of all constituents. • Put in place a simplified regulatory system for clinical research networks.	• A national clinical research system will be in place that creates data on effectiveness, outcomes, and quality of care and moves those data into the community rapidly. • A sustained efficient infrastructure will be in place that can rapidly initiate large clinical trials. • Scientific information will be made available to patients, families, and advocacy groups.
	Intermediate level of difficulty	
• Establish repositories of biological specimens and standards for collection. • Standardize nomenclature, data standards, core data, and forms for most major diseases. • Start a library of these elements shared between the institutes and NLM. • Develop efficient network administration infrastructure at the NIH. • Develop standards for capturing images for research.	• Data standards will be shared across all NIH institutes. • Funding mechanisms will be evaluated to determine which are most efficient.	• NIH, CMS, FDA, DOD, and CDC will have agreed on a single medical nomenclature with national data standards. • Data standards will be updated in real time through networks. • There will be a national repository of images and samples. • There will be a list of critical national problems. • The most efficient network funding mechanisms will be in place across the NIH.
	Highest level of difficulty	
• Create NIH standards that provide a "safe haven" for clinical research. • Inventory and evaluate existing public-private partnerships, networks, clinical research institutions, and regulatory systems. • Establish forums of all stakeholders. • Establish standards for and pilot the creation of a National Clinical Research Corps. • Offer demonstration and planning grants to those wanting to enhance, evaluate, or develop model networks.	• NIH standards that provide a safe haven will be in place. • FDA and CMS regulations and ethics will be harmonized. • Mechanisms for public-private partnerships will be in place. • The National Clinical Research Corps will have 100,000 members. • Standards will be shared across the NIH.	• Participation in research will be a professional standard taught in all health professions schools. • Study of, evaluation of, and training in clinical research will be a part of the curriculum of every medical school, nursing school, and school of pharmacy. • Clinical research practices will be documented and updated regularly to maintain a safe haven. • Clinical research networks will provide detailed training about network-specific issues.

Note. CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare & Medicaid Services; DOD, US Department of Defense; FDA, US Food and Drug Administration; NLM, National Library of Medicine.
Source: National Institutes of Health.

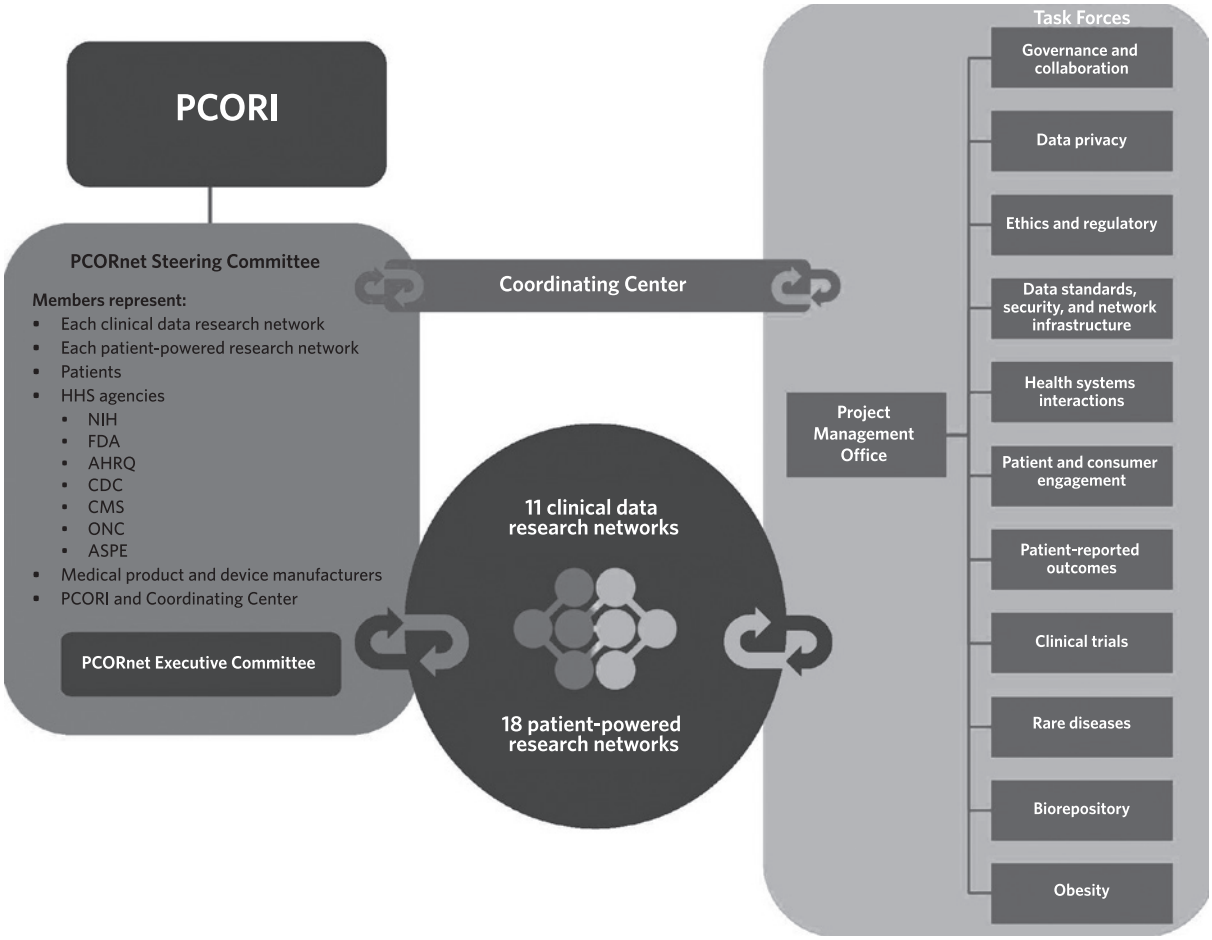
to replace randomized clinical trials; instead, it represents a complementary effort that is designed to engage multiple stakeholders and to allow a diverse array of otherwise impracticable designs to be implemented. Ultimately, PCORnet may allow us to conduct more cost-efficient clinical trials, thus answering research questions more rapidly and at a lower cost.

The Network

The structure of PCORnet is depicted in Figure 1. The primary entities are 11 clinical data research networks (CDRNs) and 18 patient-powered research networks (PPRNs). These networks are served by the PCORnet Coordinating Center, which is led by the Harvard Pilgrim Health Care Institute and the Duke Clinical Research Institute. The entire consortium is further organized into 11 task forces that will develop the network's standards and operating principles. Our goal is to achieve significant functionality by September 2016.

CDRNs. The CDRNs encompass much of the United States (Table 2). Each network represents a unique partnership of 2 or more health systems and must have full access to the EHRs of at least 1 million patients. Some networks include whole cities (eg, New York and Chicago), while others are state consortia (the Greater Plains Collaborative network, which involves 7 states), large university consortia (the campuses of the University of California form one network, and there is a mid-Atlantic consortium consisting of the University of Pittsburgh, Johns Hopkins University, Penn

FIGURE 1.
Schematic Showing Organization of the Patient-Centered Outcomes Research Network (PCORnet)



Note. AHRQ, Agency for Healthcare Research and Quality; ASPE, Assistant Secretary for Planning and Evaluation; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare & Medicaid Services; FDA, US Food and Drug Administration; HHS, US Department of Health and Human Services; NIH, National Institutes of Health; ONC, Office of the National Coordinator for Health Information Technology; PCORI, Patient-Centered Outcomes Research Institute.
Source: Adapted with permission of the Patient-Centered Outcomes Research Institute.

State College of Medicine, and Temple University School of Medicine), a consortium of 8 children's hospitals (led by the Children's Hospital of Philadelphia), and a consortium with a single university (Vanderbilt University) tied to an extensive regional network. These CDRNs will provide capacity for amassing data on common diseases in very large populations, as well as data on rare diseases in cohorts that are smaller but still sufficiently large to conduct meaningful clinical trials and observational studies.

PPRNs. In contrast to CDRNs, PPRNs are led by patients and patient advocates who have an intense interest in a specific disease; half of the PPRNs focus on rare diseases and half focus on common diseases (Table 3). Some offer extensive and well-characterized registries and biobanks, whereas others are marked by groups of enthusiastic, active patients who may be relatively inexperienced with regard to data collection and analysis but who share a deep commitment to advancing knowledge through clinical research.

The Coordinating Center. The PCORnet Coordinating Center provides technical and logistical support and works closely with PCORI to guide the consortium toward milestones that will allow the network to produce reliable research results at a fraction of current costs. The Coordinating Center is a virtual entity led by the Harvard Pilgrim Health Care Institute and the Duke Clinical Research Institute; it also has significant hubs at the Brookings Institution (focused on policy), AcademyHealth (focused on support for methods), Johns Hopkins University (focused on ethics), and America's Health Insurance Plans.

The steering committee. The steering committee includes representatives from patient advocacy groups, industry, and multiple government agencies, including the FDA, the NIH, the Centers for Medicare & Medicaid Services, and the Office of the National Coordinator for Health Information Technology. All PCORnet proceedings are public, and an explicit goal of the project is to enable nonfunded groups to work with the network in conducting both interventional clinical trials and observational studies.

TABLE 2.
Patient-Centered Outcomes Research Network (PCORnet) Clinical Data Research Networks (CDRNs)

Network	Organization(s)	Principal investigator	Clinical conditions of interest		Populations covered
			High prevalence	Rare	
Accelerating Data Value Across a National Community Health Center Network (ADVANCE)	Oregon Community Health Information Network	Jennifer DeVoe, DPhil, MD	Diabetes mellitus	HIV/hepatitis C coinfection	Underserved, rural, urban, rare disorders, children, minority, other vulnerable populations
Chicago Area Patient Centered Outcomes Research Network (CAPriCORN)	Chicago Community Trust	Terry Mazany, MA, MBA	Anemia, asthma	Sickle cell disease; recurrent *Clostridium difficile* colitis	Underserved, urban, rare disorders, children, geriatric, minority
Greater Plains Collaborative (GPC)	University of Kansas Medical Center	Lemuel Waitman, PhD	Breast cancer	Amyotrophic lateral sclerosis	Underserved, rural, urban, rare disorders, children, geriatric, minority, disabled, other vulnerable populations
Kaiser Permanente and Strategic Partners Patient Outcomes Research To Advance Learning (PORTAL) Network	Kaiser Foundation Research Institute	Elizabeth A. McGlynn, PhD	Colorectal cancer	Severe congenital heart disease	Underserved, rural, urban, rare disorders, children, geriatric, minority, disabled
Louisiana CDRN (LACDRN)	Louisiana Public Health Institute	Anjum Khurshid, PhD, MPAff, MBBS	Diabetes mellitus	Sickle cell disease; rare cancers	Underserved, rural, urban, rare disorders, children, geriatric, minority, disabled, other vulnerable populations
Mid-South CDRN	Vanderbilt University	Russell Rothman, MD, MPH	Coronary heart disease	Sickle cell disease	Underserved, rural, urban, rare disorders, children, geriatric, minority, disabled, other vulnerable populations
National Pediatric Learning Health System (PEDSnet)	Children's Hospital of Philadelphia	Christopher B. Forrest, MD, PhD	Inflammatory bowel disease	Hypoplastic left heart syndrome	Underserved, urban, rare disorders, children, minority
New York City Clinical Data Research Network (NYC-CDRN)	Weill Medical College of Cornell University	Rainu Kaushal, MD, MPH	Diabetes mellitus	Cystic fibrosis	Underserved, urban, rare disorders, children, geriatric, minority, disabled, other vulnerable populations
Patient-oriented SCAlable National Network for Effectiveness Research (pSCANNER)	University of California, San Diego	Lucila Ohno-Machado, MD, MBA, PhD	Congestive heart failure	Kawasaki disease	Underserved, urban, rare disorders, children, geriatric, minority, disabled
PaTH: Towards a Learning Health System in the Mid-Atlantic Region (formerly P2aTH)	University of Pittsburgh	Rachel Hess, MD, MS	Atrial fibrillation	Idiopathic pulmonary fibrosis	Underserved, rural, urban, rare disorders, children, minority, other vulnerable populations
Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS)	Harvard University	Kenneth Mandl, MD, MPH	Osteoarthritis	Pulmonary arterial hypertension	Underserved, rural, urban, rare disorders, children, geriatric, minority, disabled, other vulnerable populations

Note. Full descriptions of CDRNs are available on the PCORnet Web site: http://www.pcornet.org/clinical-data-research-networks/.

PCORnet task forces. The PCORnet task forces provide a venue for coordinating efforts across CDRNs and PPRNs. Each task force includes both patients and professional experts who are representatives from the constituent networks. Together, CDRNs, PPRNs, and task forces constitute a national "research fabric" that includes patients as decision makers on questions of priorities, design, conduct, and dissemination.

Major Challenges

The overall goal of PCORnet is to conduct clinical research more quickly, to improve reliability and quality, and to significantly reduce costs. However, such an ambitious project comes with a number of potential impediments, and several central challenges have been identified, including extraction and harmonization of data extracted from multiple different EHRs, creation of a common data model, ethical and regulatory issues posed by cluster-randomized designs and comparative effectiveness studies, and methods for engaging patients and consumers. The task forces are working hard to address these challenges, but due to the short timeline for development of the network, some choices about how to organize a clinical research network must be made in the absence of empirical proof of best

TABLE 3.
Patient-Centered Outcomes Research Network (PCORnet) Patient-Powered Research Networks (PPRNs)

Network	Organization	Principal investigator	Condition(s)	Proposed population
Non–rare disease PPRNs				
Multiple Sclerosis Patient-Powered Research Network	Accelerated Cure Project for Multiple Sclerosis	Robert McBurney, BSc, PhD	Multiple sclerosis	20,000
Sleep Apnea-Patient Centered Outcomes Network (SA-PCON)	American Sleep Apnea Association	Susan Redline, MD, MPH	Sleep apnea	50,000
ImproveCareNow: A Learning Health System for Children with Crohn's Disease and Ulcerative Colitis	Cincinnati Children's Hospital Medical Center	Peter Margolis, MD, PhD	Pediatric Crohn disease and ulcerative colitis	15,000
COPD Patient Powered Research Network	COPD Foundation	Richard Mularski, MD, MS	Chronic obstructive pulmonary disease	100,000
CCFA Partners Patient Powered Research Network	Crohn's and Colitis Foundation of America	R. Balfour Sartor, MD	Inflammatory bowel disease (Crohn disease and ulcerative colitis)	30,000
ARthritis patient Partnership with comparative Effectiveness Researchers (AR-PoWER PPRN)	Global Health Living Foundation	Seth Ginsberg, BS	Arthritis (rheumatoid arthritis, spondyloarthritis), musculoskeletal disorders (osteoporosis), and inflammatory conditions (psoriasis)	50,000
Mood Patient-Powered Research Network	Massachusetts General Hospital	Andrew Nierenberg, MD	Major depressive disorder and bipolar disorder	50,000
Health eHeart Alliance	University of California, San Francisco	Mark Pletcher, MD, MPH	Cardiovascular health	100,000
American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network (ABOUT Network)	University of South Florida	Rebecca Sutphen, MD	Hereditary breast and ovarian cancer	17,000
Rare disease PPRNs				
ALD Connect	ALD Connect, Inc.	Florian Eichler, MD	Adrenoleukodystrophy	3,000
NephCure Kidney Network for Patients with Nephrotic Syndrome	Arbor Research Collaborative for Health	Bruce Robinson, MD, MS	Primary nephrotic syndrome (focal segmental glomerulosclerosis, minimal change disease, and membranous nephropathy), multiple sclerosis	1,250
Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium	Duke University	Laura Schanberg, MD	Juvenile rheumatic disease	9,000
Rare Epilepsy Network (REN)	Epilepsy Foundation	Janice Buelow, PhD, RN	Aicardi syndrome, Lennox-Gastaut syndrome, Phelan-McDermid syndrome, hypothalamic hamartoma, Dravet syndrome, tuberous sclerosis	1,500
Community-Engaged Network for All (CENA)	Genetic Alliance, Inc.	Sharon Terry, MA	Alström syndrome, dyskeratosis congenital, Gaucher disease, hepatitis, inflammatory breast cancer, Joubert syndrome, Klinefelter syndrome and associated conditions, metachromatic leukodystrophy, pseudoxanthoma elasticum, psoriasis	50–50,000
PI Patient Research Connection: PI-CONNECT	Immune Deficiency Foundation	Kathleen Sullivan, MD, PhD	Primary immunodeficiency diseases	1,250
DuchenneConnect Patient-Report Registry Infrastructure Project	Parent Project Muscular Dystrophy	Holly Peay, MS	Duchenne and Becker muscular dystrophy	4,000
Phelan-McDermid Syndrome Data Network	Phelan-McDermid Syndrome Foundation	Megan O'Boyle, BA	Phelan-McDermid syndrome	737
Vasculitis Patient Powered Research Network	University of Pennsylvania	Peter Merkel, ME, MPH	Vasculitis	500

Note: Full descriptions of PPRNs are available on the PCORnet Web site: http://www.pcornet.org/patient-powered-research-networks/.

practices. For example, should a central institutional review board (IRB) be used, or should IRB reciprocity be required or encouraged? In most cases, a range of options will be available, although in some key areas a PCORnet-wide standard approach will be needed to construct a functional national network.

Data interoperability. Despite the promise of EHRs, considerable work remains before interoperable data will be available across PCORnet. A specific approach has been developed that will use the software application PopMedNet to produce data tables for each network, based on common data element definitions and models. These data tables will include basic information about demographic characteristics, diagnoses, medications, procedures, and events. This approach constitutes a substantial challenge, given the documented variability in EHRs both within and among health systems; however, we have reason for confidence thanks to the Mini-Sentinel project (a pilot program for the Sentinel Initiative) [9, 10], which used a distributed data network to amass tens of millions of records (mostly from payers) to conduct massive postmarketing surveillance. Indeed, the integration of comprehensive follow-up data from insurance claims (almost all health care transactions are recorded for the duration of coverage) and deep patient data from integrated health systems—comprising comprehensive information about demographic characteristics, diagnoses, symptoms, laboratory data, imaging, prescriptions, procedures, and clinical and patient-reported outcomes—would provide a comprehensive platform for both observational and interventional research.

Disruptions to the current system. Even after data are successfully aggregated, many of the most important questions in the realm of comparative effectiveness research will require active intervention and will often include an element of randomization. At the same time, health system administrators and clinicians continue to express concerns about unsustainable workloads and mounting demands for efficiency in health care delivery. In an increasing number of clinical research projects, the selection of priorities and research design have been consonant with health system goals, which can yield impressive efficiencies in research conduct [11]. Unfortunately, research regarding many important questions will inevitably be disruptive to health systems, and a number of research procedures—including consent—are seen as intrusive, expensive, and burdensome to the clinical care system. Therefore a key component of the PCORnet effort is fostering a sense of community around the shared understanding that continuous learning is a fundamental obligation of health systems, clinicians, and health system administrators.

Emerging issues related to research permissions and oversight present additional problems that must be addressed. The division between practice and research, which is currently being eroded by learning health system concepts, calls into question traditional views of regulation based on the ethical principles enunciated in 1979 in the Belmont Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research [12]. However, well-documented delays in the initiation of clinical research [13] can be ameliorated only by introducing new approaches on a broad scale. Such approaches include enhancement of the role for centralized or shared review of protocols by institutional review boards, the use of modified and simplified consent, and the implementation of oversight structures that are based on levels of risk rather than artificial distinctions between quality improvement and research.

Adapting to patient-centered research. The incorporation of patients into every phase of research is a new and evolving concept. In some patient communities—such as patients with HIV/AIDS, breast cancer, cystic fibrosis, or multiple myeloma—patients and their advocates are driving research agendas in full partnership with investigators [14]. Many other communities are just beginning to coalesce, and PPRNs are meant to provide a venue for the development of best practices for patient involvement.

Communication. Finally, communication is a major issue for PCORnet and its constituents. Central to the PCORnet effort is the widespread adoption of a common cause and the broad sharing of best practices across its 29 networks, thousands of investigators, and millions of patients. Reconfiguring the clinical research system will require the creation of multimedia materials, user-friendly Web portals, thoughtful approaches to social media, and systems of human contact that create efficiencies across a system that until now has been disorganized and siloed. Significant efforts will be applied to the creation of a publicly available, Web-based "living textbook" [15] designed to harness and combine creative input from thousands of interested people, while at the same time providing high-quality, curated content on multiple aspects of pragmatic clinical research.

Clinical Trials and Observational Studies

The success of PCORnet will provide an unprecedented platform for both observational studies and clinical trials. The massive size and distributed design of PCORnet should make it possible to improve the quality of published observational studies. Methods can be considered and refined by a national "brain trust" to control as best as possible for the many issues that often cause observational studies to have irreproducible results. When an interesting result is observed, it should be possible to rapidly attempt to replicate that finding in a different network.

The Clinical Trials Task Force will scrutinize every step in the clinical trial system to design an approach that can meet the demands for dramatically increased evidence generation and substantially reduced costs. Examples include the ability to prioritize research ideas through massive crowdsourcing efforts, which will ensure that the problems being addressed are of keen interest to patients who will volunteer for studies. Equally important is being able to leverage

mature, interoperable EHR systems and foster the capacity to simulate trial results, find patients, automate baseline data and outcome collection, and follow patients across networks.

Conclusion

PCORnet is meant to be a transformative new national platform for conducting patient-centered comparative effectiveness research. Our hope is that by involving all constituents in the formulation and construction of the network over the next 18 months, we will be able to create a network that the NIH, industry, and PCORI itself can use to increase the production of reliable evidence that can support decisions about health and health care delivery—potentially by at least an order of magnitude. NCMJ

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References

1. Selby JV, Lipstein SH. PCORI at 3 years—progress, lessons, and plans. N Engl J Med. 2014;370(7):592-595.
2. National Research Council; Olsen L, Aisner D, McGinnis JM, eds. The Learning Healthcare System: Workshop Summary (IOM Roundtable on Evidence-Based Medicine). Washington, DC: The National Academies Press, 2007.
3. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA. 2009;301(8):831-841.
4. Sung NS, Crowley WF Jr, Genel M, et al. Central challenges facing the national clinical research enterprise. JAMA. 2003;289(10):1278-1287.
5. Clinical Trials Transformation Initiative (CTTI). What we do: innovation through collaboration. CTTI Web site. http://www.ctti-clinicaltrials.org/what-we-do. Accessed February 27, 2014.
6. Yusuf S, Mehta SR, Díaz R, et al. Challenges in the conduct of large simple trials of important generic questions in resource-poor settings: the CREATE and ECLA trial program evaluating GIK (glucose, insulin and potassium) and low-molecular-weight heparin in acute myocardial infarction. Am Heart J. 2004;148(6):1068-1078.
7. Zerhouni E. Medicine. The NIH Roadmap. Science. 2003;302(5642):63-72.
8. Zerhouni EA, Alving B. Clinical and translational science awards: a framework for a national research agenda. Transl Res. 2006;148(1):4-5.
9. Platt R, Wilson M, Chan KA, Benner JS, Marchibroda J, McClellan M. The new Sentinel Network—improving the evidence of medical-product safety. N Engl J Med. 2009;361(7):645-647.
10. Behrman RE, Benner JS, Brown JS, McClellan M, Woodcock J, Platt R. Developing the Sentinel System—a national resource for evidence development. N Engl J Med. 2011;364(6):498-499.
11. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. N Engl J Med. 2013;368(24):2255-2265.
12. Solomon MZ, Bonham AC, eds. Ethical oversight of learning health care systems. Hastings Cent Report Special Report. 2013;43(1):S1-S44.
13. Abbott D, Califf R, Morrison BW, Pierre C, Bolte J, Chakraborty S. Cycle time metrics for multisite clinical trials in the United States. Ther Innov Regul Sci. 2013;47(2):152-160.
14. Gallin EK, Bond E, Califf RM, et al. Forging stronger partnerships between academic health centers and patient-driven organizations. Acad Med. 2013;88(9):1220-1224.
15. NIH Collaboratory, Health Care Systems Research Collaboratory. Rethinking clinical trials: a living textbook of pragmatic clinical trials. NIH Collaboratory Web site. https://www.nihcollaboratory.org/wiki/Pages/Home.aspx. Accessed March 20, 2014.